TRANSMITTAL
FORM

(to be used for all correspondence after initial filing)

Application Number	10/509,627	
Filing Date	09/29/2004	
First Named Inventor	Peggy Wingard et al.	
Art Unit	TBD	
Examiner Name	TBD	
Total Number of Pages in This Submission	Attorney Docket Number	006050.00067

ENCLOSURES (check all that apply)

<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): PTO/SB/08a; PTO/SB/08b; 1 foreign reference and 8 non-U.S. patent documents Search Report for EP 02 79 9315 dated 2/17/2005
Remarks		

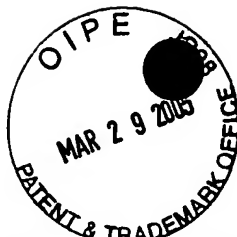
SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm	Banner & Witcoff, LTD.		
Signature			
Printed Name	Paul M. Rivard		
Date	March 29, 2005	Reg. No.	43,446

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
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This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	
Peggy Wingard et al.	:	Confirmation No.: 2806
	:	
Application No. 10/509,627	:	Group Art Unit: TBD
	:	
Filed: September 29, 2004	:	Examiner: TBD
	:	
For: PHARMACEUTICAL	:	
COMPOSITIONS CONTAINING	:	Atty Docket: 006050.00067
WATER-SOLUBLE PRODRUGS	:	
OF PROPOFOL AND METHODS	:	
OF ADMINISTERING SAME	:	

INFORMATION DISCLOSURE STATEMENT

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Sir:

Pursuant to the duty of disclosure under 37 CFR §§ 1.56 and 1.97-1.98, the documents listed on the attached forms PTO/SB/08a and PTO/SB/08b are being brought to the attention of the Examiner in charge of the above-identified application. Copies of the foreign document and the non-U.S. patent literature documents are enclosed.

A copy of the European Search Report, which issued for EP 02 79 9315 on February 17, 2005, for a related European application, is attached.

The Examiner is respectfully requested to initial the spaces adjacent each document's entry on forms PTO/SB/08a and PTO/SB/08b and to return a copy of the initialed forms to confirm that the documents have been considered and have been officially made of record in this application.

If the Examiner has any questions or wishes to discuss this application, the Examiner is invited to telephone the undersigned representative at the number set forth below.

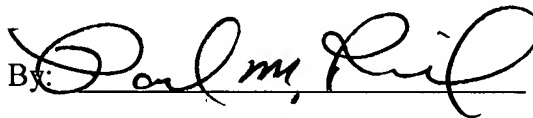
The accompanying Information Disclosure Statement is being filed before the issuance of a first action. Therefore, no fee is believed due at this time. However, the Commissioner is authorized to charge any fees that may be required to our Deposit Account No. 19-0733.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Date: March 29, 2005

1001 G Street N.W.
11th Floor
Washington, D.C. 20001
(202) 824-3000

By: 

Paul M. Rivard
Registration No. 43,446



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Substitute for form 1449A/PTO

(Use as many sheets as necessary)

Sheet	1	of	2
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Complete if Known

Application Number	10/509.627
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<i>Filing Date</i>	09/29/2004
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First Named Inventor	Peggy Wingard et al.
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Art Unit	TBD
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Examiner Name	TBD
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Attorney Docket Number	006050.00067
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U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

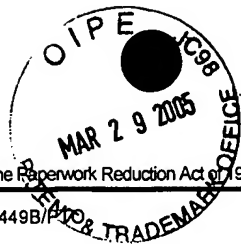
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**Examiner
Signature**

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.¹ Applicant's unique citation designation number (optional).² See Kinds codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.⁶ Applicant is to place a check mark here if English language Translation is attached.

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PTO/SB/08b(08-03)

Approved for use through 07/31/2006. OMB 0651-0031

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 2 of 2

Complete if Known

Application Number	10/509,627
Filing Date	09/29/2004
First Named Inventor	Peggy Wingard et al.
Art Unit	TBD
Examiner Name	TBD
Attorney Docket Number	006050.00067

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		SHAO, XINLI; LI, HONG; WHITE, PAUL F.; KLEIN, KEVIN W.; KULSTAD, CHRISTINE; AND OWENS, ANDREW, "Bisulfite-Containing Propofol: Is it a Cost-Effective Alternative to Diprivan™ For Induction Of Anesthesia?," Anesthesia and Analgesia, vol. 91, October 2000, pgs. 871-875	
		FARINOTTI, R., "Interactions physicochimiques et mode de conservation du Diprivan®, Physicochemical interactions and mode of storage of Diprivan®, Annales Francaises D'Anesthesie et de Reanimation, Masson, Paris, France, vol. 13, no. 4, 1994, pgs. 453-456	
		HAN, JIHONG; DAVIS, STANLEY S; AND WASHINGTON, CLIVE, "Physical properties and stability of two emulsion formulations of propofol," International Journal of Pharmaceutics, vol. 215, March 14, 2001, pgs. 207-220	
		HART, B, "Diprivan: a change of formulation," European Journal of Anaesthesiology, vol. 17, 2000, pgs. 71-73	
		MANGIAMELI, S.; CALABRESE, V.; CANTARELLA, G.; MILAZZO, G.; NICOLOSI, D.; AND RIZZA, V., "Compatibility of reduced glutathione (GSH) with different solutions currently used in anesthesia and reanimation," Minerva Anesthesiologica, vol. 61, 1995, pgs 407-409	
		CRAIG, DOUGLAS B., "Preservatives in propofol," Canadian Journal of Anesthesiology, vol. 45, no. 9, 1998, page 913	
		LEKAMP, JONATHAN E., AND DOBESH, PAUL P., "Propofol and Too Much Sulfite?," Chest, vol. 118, no. 1, July 2000, page 277	
		BAKER, MAX T., "Yellowing of metabisulfite-containing propofol emulsion," American Journal of Health-System Pharmacy, vol. 58, June 1, 2001, pgs 1042-1047	

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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Correspondence

"Preservatives" in propofol

To the Editor:

The addition of 0.005% disodium edetate to the formulation of propofol was mandated by the United States Food and Drug Administration (FDA) in 1997. Disodium edetate, in this concentration, can be expected to retard microbial growth, but not to confer complete antimicrobial "preservation".¹ This change has not been required by the Health Protection Branch (HPB) in Canada.

Propofol preparations support microbial growth² and outbreaks of postoperative infection have been linked to extrinsic contamination of the agent.^{3,4} There are no reports from Canada.

The importance of using strict aseptic techniques when drawing up propofol is emphasized widely. In addition, the interval between drug withdrawal and administration should be as short as possible, < 6 hr for single dose injections and 12 hr for continuous infusions (Propofol Product Monographs). The HPB is aware of the FDA-mandated change, but has decided not to follow their example.⁵ Reasons include- 1) concern that the presence of the "preservative" may encourage complacency and an inappropriate relaxing of the required strict aseptic handling practices; 2) knowledge that correct use of the product, as labelled (i.e. following strict aseptic technique) will prevent complications related to extrinsic contamination; 3) lack of evidence confirming a benefit from the US change in formulation; 4) absence of Canadian reports of infections due to propofol contamination; and 5) lack of evidence confirming the disodium edetate addition does not create an independent hazard.⁵

The merits of including a preservative in propofol formulations remain to be determined. Intuition suggests that a "partially preserved" product should offer a benefit over a product without preservatives which has infectious risks linked to extrinsic contamination, this has not been demonstrated and the absence of risk from the added preservative has not been confirmed. HPB deserves credit for its careful approach on this issue.

Douglas B. Craig MD FRCPC
Manitoba, Canada

REFERENCES

- 1 Sklar GE. Propofol and postoperative infections. *Ann Pharmacother* 1997; 31: 1521-3.
- 2 Tessler M, Dascal A, Gioseffini S, Miller M, Mendelson J. Growth curves of *Staphylococcus aureus*, *Candida albicans*, and *Moraxella osloensis* in propofol and other media. *Can J Anaesth* 1992; 39: 509-11.
- 3 Bennett SN, McNeil MM, Bland LA, et al. Postoperative infections traced to contamination of an intravenous anesthetic, propofol. *N Engl J Med* 1995; 333: 147-54.
- 4 Kuehnert MJ, Webb RM, Jochimsen EM, et al. *Staphylococcus aureus* bloodstream infections among patients undergoing electroconvulsive therapy traced to breaks in infection control and possible extrinsic contamination by propofol. *Anesth Analg* 1997; 85: 420-5.
- 5 Personal Communication. Dr. C. Petersen, CNS Division, Health Protection Branch. Health Canada. March 1998.

End-tidal CO₂ after CO₂ embolism

To the Editor:

Rudston-Brown and colleagues described their interesting findings concerning the haemodynamic state and gas exchange after gas embolism with CO₂ vs He in pigs.¹ The authors found more severe deleterious effects with He than with CO₂ embolism and a decrease in P_{ET}CO₂ was associated with both conditions. However, in disagreement with their results, previous experimental studies^{2,3} demonstrated an initial increase in P_{ET}CO₂ after CO₂ embolism, mostly after the injection of rapid bolus of small volumes of CO₂. This may occur as a result of the excretion of CO₂ by the lungs, after its rapid absorption into the blood. In addition, some anecdotal cases^{4,5} confirm the observations made in the mentioned experimental settings. It is possible that the adjusting of the mechanical ventilation, as described in the study by Rudston-Brown *et al.* may have increased CO₂ excretion, leading to lower P_{ET}CO₂ levels. Since CO₂ embolism presents some particular characteristics, clinical anaesthetists should be aware of this transient increase in P_{ET}CO₂ levels after CO₂ embolism in order to make an early diagnosis.

Jose Eduardo Tanus-Santos MD MSC
Department of Pharmacology